

Ames# 96-014

NASA-CR-205327

Progress Report and Statement of Work

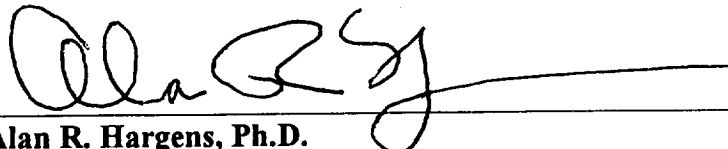
for Continuation of the Cooperative Agreement entitled

**EXERCISE WITHIN LBNP TO PRODUCE
ARTIFICIAL GRAVITY**

between

**NASA Ames Research Center
Moffett Field, CA 94035-1000**

and

**The Regents of the University of California
University of California at San Diego
Office of Contract and Grant Administration, 0934
9500 Gilman Drive
La Jolla, CA 92093-0934****Business Contact:****Martha Obermeier (619) 534-0242****Contract and Grant Officer:****Bettye R. Albritton (619) 534-3330****Principal Investigator:****Alan R. Hargens, Ph.D.
Adjunct Professor of Orthopaedics
University of California
San Diego, CA 92093-0022****Period of Performance:****12-1-95 to 11-30-96****Grant Number****NCC2-852**

Alan R. Hargens, Ph.D.**Adjunct Professor of Orthopaedics****Date**

10/85

OFFICIAL AUTHORIZED TO SIGN FOR INSTITUTION:

Roger D. Meyer, Associate Dean for Administration**Date**

10/17/95

PROGRESS REPORT

a. Lower body negative pressure exercise during bed rest maintains orthostatic tolerance.

Recent results:

Integrated physiologic countermeasures are needed to maintain orthostatic tolerance after spaceflight or bed rest. We hypothesized that supine exercise during LBNP would prevent bed rest-induced loss of orthostatic tolerance by preventing hemoconcentration. In a study conducted jointly with NASA Johnson Space Center and the University of Texas Medical Branch, Galveston, TX, fifteen male subjects underwent 5 days of 6° head-down bed rest: 5 control subjects did not exercise, and 10 performed 30 min/day of supine interval treadmill exercise at intensities up to 90% $\text{VO}_{2\text{peak}}$. One body weight of footward force was generated by 55 ± 3 mm Hg LBNP during supine exercise on a vertical treadmill. Pre- and post-bed rest orthostatic tolerance was assessed as time to presyncope during 80° head-up tilt (30 min max). Heart rate and arterial blood pressure were measured by standard methods during head-up tilt. Hematocrit quantified hemoconcentration. Mean head-up tilt tolerance was unchanged in the subjects who performed 30 min/day LBNP exercise during bed rest (pre: 25.9 ± 2.8 min, $\bar{X} \pm \text{SE}$; post: 28.2 ± 1.8 min; NSD). In contrast, tilt tolerance time in control subjects decreased from 27.3 ± 2.7 min to 22.4 ± 4.0 min ($p < 0.05$). Hematocrit increased from 41.8 ± 1.1 to $45.0 \pm 1.0\%$ in the control group during 5 days of bed rest, indicating substantial hemoconcentration. Hematocrit did not increase significantly in the group performing LBNP exercise (42.8 ± 0.8 vs. $43.5 \pm 0.8\%$; NSD). The two groups exhibited similar mean heart rates and arterial blood pressures during orthostasis after bed rest.

Significance:

These results indicate that LBNP exercise during bed rest prevents hemoconcentration, which in turn, may help maintain orthostatic tolerance.

b. A daily, 30-minute bout of interval treadmill exercise with lower body negative pressure does not maintain exercise capacity during bed rest.

Recent results:

We have shown previously that supine exercise during lower body negative pressure (LBNP) can produce similar footward forces and heart rate responses as upright exercise. In this study, we evaluated the effectiveness of a high intensity, interval exercise treadmill protocol to maintain peak oxygen uptake ($\text{VO}_{2\text{peak}}$) during 5 days of 6° head-down bed rest. The 30-minute exercise protocol (40 to 90% $\text{VO}_{2\text{peak}}$) was performed once daily while subjects ran in the supine position against LBNP adjusted to produce one body weight (55 ± 3 mm Hg). $\text{VO}_{2\text{peak}}$ was determined using a graded upright treadmill test before and immediately after bed rest in 7 control subjects (no exercise training) and 10 exercise subjects (daily exercise). For the control group, $\text{VO}_{2\text{peak}}$ decreased for 6 out of 7 subjects (45.6 ± 2.0 , mean \pm S.E. to 42.6 ± 1.4 ml/kg/min). For the exercise group, $\text{VO}_{2\text{peak}}$ decreased for 8 out of 10 subjects (48.7 ± 2.0 to 45.8 ± 2.3 ml/kg/min). Both $\text{VO}_{2\text{peak}}$ values ($P = 0.29$) and the heart rate response to the graded exercise levels ($P = 0.81$) did not differ between groups.

Significance:

Our results suggest that a longer and/or more intense treadmill LBNP exercise protocol will be necessary to maintain aerobic capacity during bed rest and space flight.

c. Supine exercise with lower body negative pressure maintains upright exercise responses after bed rest.

Recent Results:

We hypothesized that daily supine exercise with LBNP would be as effective as upright exercise in maintaining upright exercise responses after 5 days of 6° head-down tilt bed rest. Twenty-four healthy men were randomly assigned to one of three groups (n=8). The control group did not exercise, the upright group performed a daily, 30-minute interval exercise protocol on a treadmill, and the LBNPEx group performed the same protocol while supine in an LBNP device (51.3 ± 0.4 mm Hg). All subjects completed a graded upright treadmill test before and immediately after bed rest at three exercise levels with measurements of heart rate, respiratory exchange ratio, and ventilation. After bed rest, only the control group had significant ($p < 0.05$) increases in heart rate (176 ± 3 pre vs. 185 ± 2 post), respiratory exchange ratio (1.03 ± 0.02 pre vs. 1.12 ± 0.03 post), and ventilation (90 ± 5 pre vs. 103 ± 5 post) by exercise level three ($\text{VO}_2 = 41 \pm 1$ ml/kg/min).

Significance:

This investigation suggests that supine exercise with LBNP is as effective as upright exercise in maintaining upright exercise responses during bed rest, and should be considered as a possible countermeasure to help sustain egress capability after space flight.

Sections a. - c. above collectively indicate that 30 minutes of supine LBNP exercise per day at 1.0 body weight footward force during bed rest maintain orthostatic tolerance, but not aerobic fitness. Greenleaf (1989) found that 30 min/day of supine cycle ergometry maintained *supine* exercise capacity, but not orthostatic tolerance. He did not measure upright exercise capacity.

Therefore, in this proposal we have increased daily exercise load to 1.2 body weights and exercise duration to 40 minutes to protect upright exercise capacity during bed rest. Preservation of bone properties constitutes additional reason for increasing exercise load and duration. Because bone is more responsive to load magnitude than to load frequency (Whalen et al., 1988), we believe 40 min is a reasonable duration of daily activity. In addition to the potential musculoskeletal and cardiovascular benefits, treadmill exercise within LBNP may activate the same neuromuscular systems as normal ambulation, which should help prevent loss of neuromuscular coordination following bed rest and space flight (Cohen et al., 1986; Dupui et al., 1992; Homick et al., 1977; Young et al., 1984). Exercise within a LBNP chamber in space may provide a safe (no Coriolis effects), inexpensive, energy efficient, and compact alternative to centrifugation during long-duration existence in microgravity.

d. Recent Publications Relevant to Cooperative Agreement

Articles

1. Parazynski SE, AR Hargens, B Tucker, M Aratow, J Styf, and A Crenshaw. Transcapillary fluid shifts in tissues of the head and neck during and after simulated microgravity. *Journal of Applied Physiology* 71:2469-2475, 1991.
2. Hargens AR, RT Whalen, DE Watenpaugh, DF Schwandt, and LP Krock. Lower body negative pressure to provide load bearing in space. *Aviation, Space, and Environmental Medicine* 62:934-937, 1991.
3. Crenshaw AG, J Fridén, L Thornell, and AR Hargens. Extreme endurance training: Evidence of capillary and mitochondria compartmentalization in human skeletal muscle. *European Journal of Applied Physiology* 63:173-178, 1991.
4. Rydevik BJ, RA Pedowitz, AR Hargens, MR Swenson, RR Myers, and SR Garfin. Effects of acute, graded compression on spinal nerve root function and structure. An experimental study of the pig cauda equina. *Spine* 16:487-493, 1991.
5. Schwandt DF, DE Watenpaugh, SE Parazynski, and AR Hargens. Dynamic inter-limb resistance exercise device for long-duration space flight. *Technology 2001*, San Jose, CA, pp 533-537, 1991.
6. Meyer J-U, N Eliashberg, and AR Hargens. Using modal analysis for noninvasive monitoring of changes in intracranial pressure. *Annual International Conference of the IEEE Engineering in Medicine and Biology Society* 13:1957-1958, 1991.
7. Wood SC, Weber RE, AR Hargens, and RW Millard. *Physiological Adaptations in Vertebrates*. New York: Marcel Dekker, 450 pp., 1992.
8. Hargens AR, DE Watenpaugh, and GA Breit. Control of circulatory function in altered gravitational fields. *Physiologist* 35:S80-S83, 1992.
9. Pedowitz RA, DH Gershuni, J Fridén, SR Garfin, BL Rydevik, and AR Hargens. Effects of reperfusion intervals on skeletal muscle injury beneath and distal to a pneumatic tourniquet. *Journal of Hand Surgery* 17A:245-255, 1992.
10. Ballard RE, M Aratow, A Crenshaw, J Styf, N Kahan, DE Watenpaugh, and AR Hargens. Intramuscular pressure measurement as an index of torque during dynamic exercise. *Physiologist* 35:S115-S116, 1992.
11. Murthy G, RJ Marchbanks, DE Watenpaugh, and AR Hargens. Increased intracranial pressure in humans during simulated microgravity. *Physiologist* 35:S184-S185, 1992.
12. Kawai Y, G Murthy, DE Watenpaugh, and AR Hargens. Cerebral blood flow velocity increases with acute head-down tilt of humans. *Physiologist* 35:S186-S187, 1992.
13. Pedowitz RA, SR Garfin, JB Massie, AR Hargens, MR Swenson, RR Myers, and BL Rydevik. Effects of magnitude and duration of compression on spinal nerve root conduction. *Spine* 17:194-199, 1992.
14. Watenpaugh DE, CW Yancy, JC Buckey, LD Lane, AR Hargens, and CG Blomqvist. Role of atrial natriuretic peptide in systemic responses to acute isotonic volume expansion. *Journal of Applied Physiology* 73:1218-1226, 1992.
15. Crenshaw AG, JR Styf, and AR Hargens. Intramuscular pressures during exercise: An evaluation of a fiber optic transducer-tipped catheter system. *European Journal of Applied Physiology* 65:178-182, 1992.
16. Hargens AR. "Developmental Adaptations to Gravity". In: *Physiological Adaptations in Vertebrates*, edited by S.C. Wood, R.E. Weber, A.R. Hargens, and R.W. Millard. New York: Marcel Dekker, pp. 213-233, 1992.
17. Parazynski SE, BJ Tucker, M Aratow, A Crenshaw, and AR Hargens. Direct measurement of capillary blood pressure in the human lip. *Journal of Applied Physiology* 74:946-950, 1993.
18. Breit GA, DE Watenpaugh RE Ballard, G Murthy, and AR Hargens. Regional cutaneous microvascular flow responses during gravitational and LBNP stresses. *Physiologist* 36:S110-S111, 1993.
19. Aratow M, RE Ballard, AG Crenshaw, J Styf, DE Watenpaugh, NJ Kahan, and AR Hargens. Intramuscular pressure and electromyography as indexes of force during isokinetic exercise. *Journal of Applied Physiology* 74:2634-2640, 1993.
20. Aratow M, SM Fortney, DE Watenpaugh, AG Crenshaw, and AR Hargens. Transcapillary fluid responses to lower body negative pressure. *Journal of Applied Physiology* 74:2763-2770, 1993.
21. Kawai Y, G Murthy, DE Watenpaugh, GA Breit, CW DeRoshia, and AR Hargens. Cerebral blood flow velocity in humans exposed to 24 h of head-down tilt. *J. Appl. Physiol.* 74:3046-51, 1993.

22. Pedowitz RA, DH Gershuni, MJ Botte, S Kuiper, BL Rydevik, and AR Hargens. The use of lower tourniquet inflation pressures in extremity surgery facilitated by curved and wide tourniquets and an integrated cuff inflation system. *Clinical Orthopaedics and Related Research* 287:237-244, 1993.
23. Nakostine M, JR Styf, S Van Leuven, AR Hargens, DH Gershuni. Intramuscular pressure varies with depth. The tibialis anterior muscle studied in 12 volunteers. *Acta Orthop. Scand.* 64:377-81, 1993.
24. Crenshaw AG, J Fridén, AR Hargens, GH Lang, and LE Thornell. Increased technetium uptake is not equivalent to muscle necrosis: scintigraphic, morphological, and intramuscular pressure analyses of sore muscles after exercise. *Acta Physiologica Scandinavica* 148:187-198, 1993.
25. Breit GA, DE Watenpaugh, RE Ballard, and AR Hargens. Acute cutaneous microvascular flow responses to whole-body tilting in humans. *Microvascular Research* 46:351-358, 1993.
26. Hargens AR, MJ Botte, MR Swenson, RH Gelberman, CE Rhoades, and WH Akesson. Local compression effects on peroneal nerve function in humans. *Journal of Orthopaedic Research* 11:818-827, 1993.
27. Watenpaugh DE, RE Ballard, MS Stout, G Murthy, RT Whalen, and AR Hargens. Dynamic leg exercise improves tolerance to lower body negative pressure. *Aviation, Space, and Environmental Medicine*, 65:412-418, 1993.
28. Murthy G, DE Watenpaugh, RE Ballard, and AR Hargens. Exercise against lower body negative pressure as a countermeasure for cardiovascular and musculoskeletal deconditioning. *Acta Astronautica*, 33:89-96, 1993.
29. Murthy G, RE Ballard, GA Breit, DE Watenpaugh, and AR Hargens. Intramuscular pressures beneath elastic and inelastic leggings. *Annals of Vascular Surgery* 8:543-548, 1994.
30. Murthy G, DE Watenpaugh, RE Ballard, and AR Hargens. Supine exercise during lower body negative pressure effectively simulates upright exercise in normal gravity. *Journal of Applied Physiology*, 76:2742-2748, 1994.
31. Hargens AR. "Recent Bed Rest Results and Countermeasure Development at NASA". In: *Inactivity and Health: Effects of Bedrest on Health*, Oxford: Blackwell, *Acta. Physiol. Scand.* 150, Suppl. 616, pp. 103-114, 1994.
32. Murthy G and AR Hargens. "Recent Advances in Space Biomedicine". In: *Recent Advances in Biomedical Engineering*, edited by DC Reddy. New Delhi: Tata McGraw-Hill, pp. 190-195, 1994.
33. Hutchinson KJ, DE Watenpaugh, G Murthy, VA Convertino, and AR Hargens. Back pain during 6° head-down tilt approximates that during actual microgravity. *Aviation, Space, and Environmental Medicine* 66:256-259, 1995.
34. Stout MS, DE Watenpaugh, GA Breit, and AR Hargens. Simulated microgravity increases cutaneous microcirculatory blood flow in the head and leg of humans. *Aviation, Space, and Environmental Medicine* 66:872-875, 1995.
35. Hargens AR and JL Villavicencio. "Mechanics of Tissue/Lymphatic Transport". In: *Biomedical Engineering Handbook*. Boca Raton: CRC Press, Inc., Chapt. 37, pp.493-504, 1995.
36. Watenpaugh, DE and AR Hargens. The Cardiovascular System in Microgravity. In: *Handbook of Physiology*, Section 4: Adaptation to the Environment. Edited by MJ Fregly and CM Blatteis, Part 4: The Gravitational Environment, Chapter 30. New York: Oxford University Press, in press, 1995.
37. Hargens AR and DE Watenpaugh. "Cardiovascular and Cardiopulmonary Function in Microgravity". In: *Biology and Space Exploration*, edited by MM Cohen and AR Hargens. New York: Plenum Press, in press, 1995.
38. Sejersted OM and AR Hargens. "Intramuscular Pressures for Monitoring Different Tasks and Muscle Conditions". In: *Motor Control VII*, edited by S Gandevia, RM Enoka, AJ McComas, DG Stuart, and CK Thomas. New York: Plenum Press, in press, 1995.
39. Hargens AR and RE Ballard. Basic principles for measurement of intramuscular pressure. *Operative Techniques in Sports Medicine* 3(4): in press, 1995.
40. Murthy G and AR Hargens. Near infrared spectroscopy: A noninvasive technique for diagnosing exertional compartment syndrome. *Operative Techniques in Sports Medicine* 3(4): in press, 1995.
41. Lillywhite HB, R Ballard, and AR Hargens. Tolerance of snakes to hypergravity. *Physiological Zoology*, accepted, 1995.
42. Chang DS, GA Breit, JR Styf, and AR Hargens. Cutaneous microvascular flow in the foot during simulated variable gravities. *American Journal of Physiology*, in review, 1995.

Patents

1. Whalen RT and AR Hargens. Exercise Method and Apparatus Utilizing Differential Air Pressure (U.S. Patent 5,133,339 issued 28 July 1992).

2. Watenpaugh DE. Self-Generated Oscillating Pressure Exercise Device. (U.S. Patent 5,356,361 issued October 1994).

Abstracts

1. Watenpaugh DE, RE Ballard, MS Stout, G Murthy, RT Whalen, and AR Hargens. Load bearing exercise against lower body negative pressure (LBNP) increases tolerance. 62nd Annual Meeting of Aerospace Medical Association, Abstract 166, May 5-9, 1991.
2. Hargens AR, RT Whalen, DE Watenpaugh, and DF Schwandt. Atmospheric pressure differentials as an alternative to rotating artificial gravity in long-duration space missions. 62nd Annual Meeting of Aerospace Medical Association, Abstract 539, May 5-9, 1991.
3. Ballard RE, M Aratow, A Crenshaw, J Styf, N Kahan, DE Watenpaugh, AR Hargens. Intramuscular pressure measurement as an index of torque during dynamic exercise. Transactions 13th Annual Meeting IUPS Commission on Gravitational Physiology, San Antonio, Texas. *The Physiologist* 34:236(25.10), 1991.
4. Murthy G, RJ Marchbanks, DE Watenpaugh, and AR Hargens. Increased intracranial pressure (ICP) in humans during simulated microgravity. Transactions 13th Annual Meeting IUPS Commission on Gravitational Physiology, San Antonio, Texas. *The Physiologist* 34:257(48.1), 1991.
5. Kawai Y, G Murthy, DE Watenpaugh, and AR Hargens. Cerebral blood flow velocity increases with acute head-down tilt of humans. Transactions 13th Annual Meeting IUPS Commission on Gravitational Physiology, San Antonio, Texas. *The Physiologist* 34:257(48.2), 1991.
6. Watenpaugh DE, SF Vissing, LD Lane, JC Buckey, BG Firth, W Erdman, AR Hargens, and CG Blomqvist. Atrial natriuretic peptide reduces leg transcapillary filtration. Transactions 13th Annual Meeting IUPS Commission on Gravitational Physiology, San Antonio, Texas. *The Physiologist* 34:261(49.11), 1991.
7. Hargens AR. Fluid shifts in humans with actual and simulated microgravity - An overview. 1991 Annual Biomedical Engineering Society, Charlottesville, VA, Abstract 19, 1991.
8. Hargens AR, DF Schwandt, SE Parazynski, and DE Watenpaugh. Dynamic inter-limb resistance exercise device for long-duration space flight. Technology 2001 Symposium, San Jose, CA, 1991.
9. Aratow M, R Ballard, A Crenshaw, J Styf, N Kahan, DE Watenpaugh, and AR Hargens. The relationship of intramuscular pressure to ankle joint torque during isokinetic exercise. *Medicine and Science in Sports and Exercise* 24 (5 Suppl.):S164 (980), 1992.
10. Rempel D, T Bloom, R Tal, A Hargens, and L Gordon. A method of measuring intracarpal pressure and elementary hand maneuvers. International Scientific Conference on Prevention of Work-Related Musculoskeletal Disorders (PREMUS), May 1992, Stockholm.
11. Pedowitz RA, MD Jacobson, BC Tryon, AR Hargens, and DH Gershuni. Muscle function deficit after tourniquet ischemia. Annual Meeting of the American Orthopaedic Society for Sports Medicine, San Diego, CA, 1992.
12. Kahan NJ, M Aratow, DE Watenpaugh, RE Ballard, J Styf, A Crenshaw, and AR Hargens. Surface EMG versus intramuscular EMG: correlations with joint torque during isometric, concentric, and eccentric exercise. FASEB Annual Meeting, FASEB Journal 6:A1237 (1737), 1992.
13. Murthy G, DE Watenpaugh, RE Ballard, RT Whalen, and AR Hargens. Footward forces and intramuscular pressures generated during exercise in supine lower body negative pressure versus upright posture. FASEB Annual Meeting, FASEB Journal 6:A1770 (4823), 1992.
14. Watenpaugh DE, GA Breit, RE Ballard, and AR Hargens. Monitoring acute whole-body fluid redistribution by changes in leg and neck volume. FASEB Annual Meeting, FASEB Journal 6:A1771 (4829), 1992.
15. Kawai Y, G Murthy, CW DeRoshia, DE Watenpaugh, GA Breit, and AR Hargens. Head-down tilt increases cerebral blood flow velocity in humans. FASEB Annual Meeting, FASEB Journal 6:A1771 (4831), 1992.
16. Breit GA, DE Watenpaugh, RE Ballard, and AR Hargens. Acute cutaneous flow and volume responses to whole-body tilting in humans. FASEB Annual Meeting, FASEB Journal 6:A1771 (4830), 1992.
17. Stout MS, DE Watenpaugh, GA Breit, and AR Hargens. The effects of simulated microgravity on regional cutaneous microcirculatory blood flow. FASEB Annual Meeting, FASEB Journal 6:A1771 (4832), 1992.
18. Pedowitz RA, BC Tryon, MD Jacobson, AR Hargens, and DH Gershuni. Differential effects of tourniquet ischemia upon tibialis anterior force with nerve or muscle stimulation. *Orthopaedic Transactions* 16:541, 1992.

19. Hargens AR, RE Ballard, M Aratow, A Crenshaw, J Styf, N Kahan, and DE Watenpaugh. Intramuscular pressure: A better tool than EMG to optimize exercise for long-duration space flight. 63rd Annual Meeting of the Aerospace Medical Association, Miami, FL, p. A6 (Abstract 29), 1992.
20. Breit GA, DE Watenpaugh, and AR Hargens. Acute effects of whole-body tilting on cutaneous microvascular flow, volume, and vasoactivity in unanesthetized humans. 17th European Conference on Microcirculation, London, UK, International Journal of Microcirculation: Clinical and Experimental 11:S56(88), 1992.
21. Watenpaugh DE, RE Ballard, GA Breit, and AR Hargens. Exercise against self-generated lower body negative pressure. The Physiologist 35:217 (43.5), 1992.
22. Breit GA, DE Watenpaugh, RE Ballard, G Murthy, and AR Hargens. Regional cutaneous microvascular flow responses during gravitational and LBNP stresses. 14th Annual Meeting of the IUPS Commission on Gravitational Physiology, Berlin, Germany, Abstract No. 5, 29 September - 2 October 1992.
23. Murthy G and AR Hargens. Intervertebral disc swelling pressures in normal gravity and microgravity. 8th Annual Meeting of the American Society for Gravitational and Space Biology, Tucson AZ, 21-24 October 1992.
24. Ballard RE, G Murthy, DE Watenpaugh, RT Whalen, and AR Hargens. Exercise against lower body negative pressure potentially simulates 1-g exercise. 8th Annual Meeting of the American Society for Gravitational and Space Biology, Tucson AZ, 21-24 October 1992.
25. Kawai Y, SC Puma, AR Hargens, and G Murthy. +Gz acceleration-induced reduction of cerebral blood flow velocity in humans with and without straining. 8th Annual Meeting of the American Society for Gravitational and Space Biology, Tucson AZ, 21-24 October 1992.
26. Kahan NJ, M Aratow, RE Ballard, JR Styf, and AR Hargens. Intramuscular fluid pressure, surface EMG, and intramuscular EMG: Correlation with joint torque during dynamic exercise. American Congress of Rehabilitation Medicine, San Francisco, CA, 13-17 November 1992.
27. Hargens AR. Cardiovascular effects of microgravity. Symposium on Far-Out Rehabilitation Medicine. American Congress of Rehabilitation Medicine, San Francisco, CA, 13-17 November 1992.
28. Parazynski SE, M Yaron, EM Eby, JA Lickteig, G Murthy, and AR Hargens. Fluid shifts induced by altitude exposure. Eighth International Hypoxia Symposium, 9-13 February 1993.
29. Styf JR, M Aratow, RE Ballard, A Crenshaw, D Watenpaugh, and AR Hargens. Intramuscular pressures and torque during isometric, concentric, and eccentric muscular activity. 39th Annual Meeting of the Orthopaedic Research Society 18:164, 15-18 February 1993.
30. Breit GA, DE Watenpaugh, RE Ballard, G Murthy, and AR Hargens. Cutaneous microvascular flow responses during head-up tilt, centrifugation, and LBNP stresses. FASEB Journal, 7:A666, 1993.
31. Hutchinson KJ, AR Hargens, G Murthy, DE Watenpaugh, VA Convertino, and PC Wing. 6° head-down tilt as a back pain model for actual microgravity. FASEB Journal, 7:A666 (3859), 1993.
32. Murthy G, RE Ballard, GA Breit, DE Watenpaugh, and AR Hargens. Inelastic compression during leg exercise increases efficiency of the skeletal muscle pump. FASEB Journal, 7:A749 (4326), 1993.
33. Murthy G, DE Watenpaugh, RE Ballard, GA Breit, and AR Hargens. LBNP exercise may simulate 1-g exercise during microgravity exposure. 10th IAA Man in Space Symposium, Tokyo, Japan, 19-23 April 1993.
34. Hargens AR. Far-out physiology: Cardiovascular adaptation in space. III World Congress of the International Society for Adaptive Medicine. Tokyo, Japan, 26-28 April 1993.
35. Ballard RE, DE Watenpaugh, GA Breit, and AR Hargens. Exercise against self-generated lower body negative pressure for use in microgravity. Aviation, Space and Environmental Medicine 64(5):458(237), 1993. (Young Investigator Certificate of Commendation Award)
36. Watenpaugh DE, GA Breit, RE Ballard, S Zietz, and AR Hargens. Vascular compliance in the leg is lower than in the neck in humans. Medicine and Science in Sports and Exercise 25(Suppl.):526, 1993.
37. Hargens AR, SM Fortney, RE Ballard, G Murthy, SMC Lee, BS Bennett, SR Ford, and DE Watenpaugh. Supine treadmill exercise during lower body negative pressure provides equivalent cardiovascular stress to upright exercise in 1 G. Aviation, Space, and Environmental Medicine 65(5):A25(147), 1994.
38. Watenpaugh DE, RE Ballard, SM Fortney, and AR Hargens. Larger waist seal area decreases the lower body negative pressure required to produce a given level of footward force. Aviation, Space, and Environmental Medicine 65(5):A25(148), 1994.
39. Styf JR, Kålebo P, and AR Hargens. Lumbar intervertebral disc heights as measured by sonography. Aviation, Space, and Environmental Medicine 65(5):A12(67), 1994.

40. DeRoshia CW, Y Kawai, G Murthy, DE Watenpaugh, GA Breit, and AR Hargens. The effect of head-down tilt induced changes in cerebral blood flow upon human performance. *Aviation, Space, and Environmental Medicine* 65(5):A28(165), 1994.
41. Watenpaugh DE, SM Fortney, RE Ballard, SMC Lee, BS Bennett, G Murthy, GC Kramer, and AR Hargens. Lower body negative pressure exercise during bed rest maintains orthostatic tolerance. *Experimental Biology (FASEB) Annual Meeting*, Anaheim CA, 24-28 April 1994.
42. Fortney SM, DE Watenpaugh, AR Hargens, RE Ballard, G Murthy, SMC Lee, BS Bennett, and SR Ford. A daily, 30-min bout of interval treadmill exercise with lower body negative pressure (LBNP) does not maintain exercise capacity during bed rest. *Experimental Biology (FASEB) Annual Meeting*, Anaheim CA, 24-28 April 1994.
43. Hargens AR. Artificial gravity countermeasures. *Musculoskeletal Responses to Space Flight panel. Space Life Sciences Symposium, National Space Grant College and Fellowship Program*, Houston, TX, 23-25 May 1994.
44. Hargens AR. Biology course video series "Biology and Space Exploration". *Research and Education panel. Space Life Sciences Symposium, National Space Grant College and Fellowship Program*, Houston, TX, 23-25 May 1994.
45. Ballard RE, DE Watenpaugh, GA Breit, G Murthy, RT Whalen, and AR Hargens. Intramuscular pressure measurement for assessing muscle function during locomotion. *Medicine and Science in Sports and Exercise* 26(5):S141(790), 1994.
46. Tipton CM, AR Hargens, KM Baldwin, V Schneider, VA Convertino, and I Kozlovskaya. Physiological adaptations and countermeasures associated with long-duration space flights. *Medicine and Science in Sports and Exercise* 26(5):S175(976), 1994.
47. Ballard RE, JR Styf, DE Watenpaugh, K Fechner, Y Haruna, NJ Kahan, and AR Hargens. Head-down tilt with balanced traction as a model for simulating spinal acclimation to microgravity. *ASGSB Bulletin* 8:19(38), 1994.
48. Watenpaugh DE, GA Breit, RE Ballard, G Murthy, and AR Hargens. Fluid redistribution and heart rate in humans during whole-body tilting, Gz centrifugation, and lower body negative pressure. *ASGSB Bulletin* 8:35(65), 1994.
49. Breit GA, DE Watenpaugh, TM Buckley, RE Ballard, G Murthy, and AR Hargens. Peripheral microvascular responses to whole-body tilting, Gz centrifugation, and lower body negative pressure. *ASGSB Bulletin* 8:66(123), 1994.
50. Lillywhite HB, RE Ballard, AR Hargens. Tolerance of snakes to hypergravity. *ASGSB B.* 8:67, 1994.
51. Hargens AR, SE Parazynski, DE Watenpaugh, M Aratow, G Murthy, and Y Kawai. Mechanism of headward fluid shift during exposure to microgravity. *Pathophysiology* 1(Suppl.):364, 1994.
52. Murthy G, WT Yost, RE Ballard, DE Watenpaugh, Y Kawai, and AR Hargens. Ultrasound as a noninvasive method to assess changes of intracranial volume and pressure during simulated microgravity. *Pathophysiology* 1(Suppl.):366, 1994.
53. Ballard RE, HB Lillywhite, and AR Hargens. Cardiovascular responses of snakes to hypergravity. *16th Annual International Gravitational Physiology Meeting*, Reno, NV, 19-24 March 1995.
54. Johnson CC and AR Hargens. Centrifuge facility for the international space station alpha. *16th Annual International Gravitational Physiology Meeting*, Reno, NV, 19-24 March 1995 (Abstract 46).
55. Torikoshi S, RE Ballard, DE Watenpaugh, G Murthy, S Bowley, WT Yost, and AR Hargens. Measurement of transcranial distance during head-down tilt using ultrasound. *16th Annual International Gravitational Physiology Meeting*, Reno, NV, 19-24 March 1995 (Abstract 85).
56. Watenpaugh DE, RE Ballard, GA Breit, EM Bernauer, CG Blomqvist, and AR Hargens. Calf venous compliance in supine posture equals that measured with head-up tilt. *16th Annual International Gravitational Physiology Meeting*, Reno, NV, 19-24 March 1995 (Abstract 91).
57. Johnson CC, AR Hargens, CE Wade. Space station biological research project. *Life Sciences and Space Medicine Conference*, Houston, TX, 3-5 April 1995, p. 14.
58. Hargens AR, RE Ballard, M Wilson, S Torikoshi, G Murthy, GA Breit, DE Watenpaugh, Y Kawai, and WT Yost. *Life Sciences and Space Medicine Conference*, Houston, TX, 3-5 April 1995, pp. 130-131.
59. Whalen RT, AR Hargens, GA Breit, and D Schwandt. Application of air pressure loading to space flight exercise and walking assistance on earth. *Life Sciences and Space Medicine Conference*, Houston, TX, 3-5 April 1995, pp. 218-219.
60. Conklin D, H Lillywhite, K. Olson, R Ballard, and A Hargens. Blood vessel reactivity in a semi-arboreal snake. *FASEB Journal* 9(3):A354(2050), 1995.

61. Lee SMC, BS Bennett, AR Hargens, DE Watenpaugh, RE Ballard, G Murthy, S Ford, and SM Fortney. Supine exercise with lower body negative pressure (LBNP) maintains upright exercise responses after bed rest. *FASEB Journal* 9(4):A873(5068), 1995.
62. Hargens AR, ST Hsieh, G Murthy, RE Ballard, and VA Convertino. Sixteen-day bedrest significantly increases plasma colloid osmotic pressure. *Aerospace Medical Association Meeting, Anaheim, CA, 7-11 May 1995*, p. A23 (Abstract 131).
63. Jensen BR, K Sjøgaard, A Hargens, and G Sjøgaard. Dissociation between intramuscular pressure and EMG during prolonged submaximal contraction. *Scandinavian Physiological Society Meeting, Copenhagen, Denmark, 19-21 May 1995*.
64. Hargens AR, GA Breit, JH Gross, DE Watenpaugh, and B Chance. Near-infrared monitoring of model chronic compartment syndrome in exercising skeletal muscle. *Combined Orthopaedic Research Societies Meeting, San Diego, CA, 6-8 November 1995*.

STATEMENT OF WORK

Bed rest studies to test efficacy of LBNP exercise concept for preventing musculoskeletal and cardiovascular deconditioning

We will undertake two 14 day bed-rest studies (6° head-down tilt bed rest, HDT) to investigate the mechanism of action and efficacy of our partial vacuum exerciser concept. These 14 day bed rest studies were chosen to simulate current microgravity exposures for Space Shuttle crew members. All human research proposed for this cooperative agreement continuation will be performed at NASA Ames Research Center, Moffett Field, CA. The Ames Human Research Facility (HRF) can accommodate 8 subjects comfortably. We will attempt to examine the same 8 subjects in both 14 day bed rest studies, randomly assigning four subjects to 40 minutes of supine running exercise per day at 1.2 body weight of footward force (60-70 mm Hg LBNP), while the remaining four subjects will constitute the nonexercise "control" group. The rationale for selection of 40 minutes of exercise per day is that aerobic fitness (ACSM Position Paper, 1990) and bone material properties (Goldstein et al., 1988; Whalen et al., 1988) should be maintained. Therefore, our interval exercise protocol will be similar to that employed by Greenleaf et al. (1989), but longer and more intense: 7 min warm-up at 40% peak oxygen uptake, followed by 3 min at 60%, 2 min at 40%, 3 min at 70%, 2 min at 50%, 3 min at 80%, 2 min at 60%, 3 min at 80%, 2 min at 50%, 3 min at 70%, 2 min at 40%, 3 min at 60%, and 5 min cool-down at 40% peak oxygen uptake (40 min total).

Four months after the first 14 day HDT study, the two groups will be reversed so that the previous nonexercise group will receive the same 40 min of supine jogging per day at 1.2 body weight (60-70 mm Hg LBNP) while the previously-exercised group will not exercise during the 14 days of HDT. This paired experimental design, where each subject is his own control, will allow for more powerful statistical comparisons. Also, if one or two subjects drop out of the studies, we will still have a total of 6-7 subjects with paired comparisons possible for each physiologic test. Besides having the subjects act as their own control, both HDT sessions will include a three day ambulatory control period to provide baseline data and a two day recovery period to monitor return of physiologic function. If important parameters such as muscle strength, urinary markers of collagen breakdown, or gait have not returned to their normal baseline values after two days, a longer period of recovery testing will be undertaken.

In the two weeks prior to the baseline control period, activity logs will be maintained on each subject, and ambulatory levels of urinary collagen breakdown markers will be established. All physiologic tests and exercise bouts will take place at the same time of day for a given subject. These tests and exercise bouts will be staggered so that sufficient time is allowed to complete the procedure. While the subjects live at the HRF, their diet will be controlled (approximately 2500-3000 kcal per day, depending on exercise level) and their body weight, fluid intake and urine outputs will be monitored. We expect that subjects will maintain a neutral or positive fluid balance, and that they will not lose weight, when performing LBNP exercise during 14 d HDT. During the entire period

of bed rest, all subjects will remain in 6° HDT except during periods for showers and exercise (0.5-1.5 h/day), when they will be horizontal (0°).

On the day before HDT bed rest, all subjects will be tested for orthostatic tolerance and upright peak oxygen uptake. Other tests on this day will include cerebral blood flow, plasma volume, leg muscle strength, and urine and gait analyses. During the recovery period, these tests will be repeated within 4 h of return to upright posture and every other day thereafter until results are within 5% of their control, baseline value. Subjects will be staggered with respect to time of HDT initiation and return to upright posture to facilitate testing. Time of day of exercise bouts and physiologic testing will be held constant for a given subject.

REFERENCES

- ACSM Position Paper. The recommended quantity and quality of exercise for developing and maintaining cardiorespiratory and muscular fitness in healthy adults. *Med. Sci. Sports Exerc.* 1990; 22:265-74.
- Goldstein SA, JL Kuhn, SJ Hollister, RW Goulet, PV Loubert, K Sweet, LS Matthews. The relationship between experimentally controlled loads and trabecular bone remodeling. *Trans. Orthop. Res. Soc.* 1988; 13:102.
- Greenleaf JE, EM Bernauer, AC Ertl, TS Trowbridge, CE Wade. Work capacity during 30 days of bed rest with isotonic and isokinetic exercise training. *J. Appl. Physiol.* 1989; 67:1820-6.
- Whalen RT, DR Carter, CR Steele. Influence of physical activity on the regulation of bone density. *J. Biomech.* 1988; 21:825-37.

Budget for Continuation Costs

DETAILED BUDGET FOR 12-MONTH CONTINUATION			FROM Dec. 1, 1995	THROUGH Nov. 30, 1996	
			DOLLAR AMOUNT REQUESTED		
PERSONNEL		EFFORT ON PROJECT	SALARY	FRINGE BENEFITS	TOTALS
NAME	TITLE				
D.E. Watenpaugh	Lab Manager	100%	54,111	13,257	67,368
R.E. Ballard	Research Associate	100%	34,065	8,346	42,411
G. Murthy	Research Associate	67%	27,074	6,633	33,707
K.J. Hutchinson	Exp. Data Assistant	100%	30,195	7,397	37,592
SUBTOTALS			\$145,445	\$35,633	\$181,078
EQUIPMENT	2 IBM compatible Pentium-based computers			4,000	
	PowerMac computer			4,000	
	Color printer			500	
	IBM compatible laser printer			500	9,000
SUPPLIES	Medical supplies			3,000	
	Gastro-intestinal function study supplies			1,215	
	Page charges			1,000	
	Reproduction services			750	
	Video and film services			750	6,715
TRAVEL					
	3 investigators to 1 scientific meeting each			2,808	2,808
NON-EQUIPMENT DIRECT COSTS					190,601
INDIRECT COSTS					49,556
EQUIPMENT COSTS					9,000
TOTAL COSTS FOR 12-MONTH CONTINUATION					\$249,157

Budget Justification**a. Personnel**

Salary support and benefits are required for ongoing employment of laboratory personnel (Ballard, Hutchinson, Murthy and Watenpaugh) and the addition of a lab assistant.

b. Equipment

A recent upgrade in the software necessary to run the Lido dynamometer requires a Pentium-based IBM compatible computer (\$2,000) and printer (\$500). The Lido dynamometer is necessary for studies of leg muscle strength and endurance. An additional Pentium-based computer is necessary to support general data acquisition

needs of the laboratory. Specifically, the orthostatic tolerance test station will require simultaneous monitoring and recording of 11 variables. A PowerMac (\$4,000) and color printer will be used to support graphic software upgrades and integrate Mac and IBM data reduction and analysis tasks.

c. Supplies

Supplies include sterile and non-sterile medical supplies (tape, Op-site, electrodes, gauze, catheter introducers, saline, syringes, Lidocaine, gloves, drapes, needles, razors, Betadine swabs, Benzoin, hydrogen peroxide, pressure tubing, 2- and 4-way stopcocks, Evan's blue dye, mouthpieces for oxygen consumption measurement, disposable temperature sensor probes, urinals, Alconox detergent, Cidex disinfectant, etc.), reproduction and film processing services, and support for journal page charges and reprint costs.

d. Travel

Travel support is requested for attendance of one scientific meeting by each of three investigators to present results from the studies proposed in this continuation. The dates and locations of the meetings to be attended are not yet known, because abstracts have not yet been submitted and accepted. However, past experience indicates that the cost for one investigator to attend a typical 4-day meeting equals approximately \$936 (\$333 airfare, \$105 registration, \$62/day hotel, \$31/day food, and \$33/day ground transportation). Therefore, the total cost for three investigators to attend one scientific meeting each is \$2,808.

e. Indirect Costs

Indirect costs of this Cooperative Agreement (26%) apply to all non-equipment line items, and are included.